## IN THE SPECIFICATION

Please delete the Title of the Invention at page 1, lines 2-3 in its entirety and replace with the following:

## LASER-INDUCED BREAKDOWN SPECTROSCOPY FOR SPECIMEN ANALYSIS

Please delete the fourth full paragraph at page 2, lines 16-18 in its entirety.

Please replace the second full paragraph at page 3, lines 10-20 as follows:

Recent surveys reveal that in 2003, breast cancer will be newly diagnosed in over 200,000 women in the United States.[[[4,5] ]] [1,2] Early diagnosis, especially before the cancer has metastasized to regional lymph nodes is essential. Breast lumps can be found by self-examining or a physical examination by a medical practitioner. Primary diagnosis is currently done using ultrasound and/or mammography tests. In the regular course of diagnosis, a breast biopsy is needed to determine whether a lump is malignant or benign. This requires that the lump, or some part thereof be first extracted by surgery and then analyzed using pathological methodology to determine whether the biopsy contains cancerous cells. Recently, imaging and molecular biology techniques have been developed for assisting with cancer diagnosis.[[[6-8]]] [3-5]

Please replace the third paragraph beginning at page 3, at line 21 continuing on to page 4, line 4, as follows:

Existing technologies for cancer detection include radiology, NMR imaging and biopsy [[,]] followed by histopathological examination. Newer methods, which are still experimental include matrix assisted laser desorption/ionization (MALDI) technique, and surface enhanced laser/desorption ionization (SELDI) technique. These different methodologies are very

expensive and can also require significant time for analyzing a sample in a laboratory. Current methods for definitive identification of malignancy within a breast can be a difficult and painful process because a sample from a suspicious tissue mass must be extracted and then analyzed to determine whether it is malignant.

Please replace the first full paragraph at page 5, lines 5-23 as follows:

An object of the invention is a laser-induced breakdown spectroscopy (LIBS) apparatus having a laser light source, a detector, and a probe for directing laser light from the laser light source to a sample *in vivo*; wherein the laser light is directable through the probe to a sample *in vivo* to generate an emission spectrum and said emission spectrum from said sample is capturable for a recording, a real-time analysis or a subsequent analysis. Another object is an apparatus further comprising a data acquisition or analysis system with optionally a separate data processor. Another object is such an apparatus in which the laser light is transmitted to the probe through a harmonic separator for directing laser light from the laser light source. Another object is such an apparatus further comprising a dichroic mirror for reflecting the laser light from the harmonic separator. Another object is such an apparatus further comprising a coupling lens for coupling the laser light at an input end of a [[multi-modal]] multi-mode optical fiber. Another object is such an apparatus wherein the emission spectrum is collected either in the same fiber or in another fiber to travel in a backward direction to a spectrometer. Another object is such an apparatus wherein the laser light source is a $CO_2$ laser, a Ruby laser, a long-pulse YAG laser, an Alexandrite laser, an ER:YAG laser, an intense pulsed light laser, a KTP laser, a diode laser, a pulse dye laser or a pulsed Nd:YAG laser. Another object is such an apparatus wherein apparatus is part of a laser scalpel.

Please replace the first full paragraph at page 6, lines 1-19 as follows:

Still another object of the invention is a laser-induced breakdown spectroscopy (LIBS) system comprising a laser light source, a detector, and a biological sample, wherein the laser light is directable to the biological sample to generate an emission spectrum and said emission spectrum from said biological sample is capturable for a recording, a real-time analysis or a subsequent analysis. ~~Another object is a system further comprising a data acquisition or analysis system with optionally a separate data processor. Another object is such a system in which the laser light is transmitted to the probe through a harmonic separator for directing laser light from the laser light source. Another object is such a system further comprising a dichroic mirror for reflecting the laser light from the harmonic separator. Another object is such a system further comprising a coupling lens for coupling the laser light at an input end of a multi-modal optical fiber. Another object is such a system wherein the emission spectrum is collected either in the same fiber or in another fiber to travel in a backward direction to a spectrometer. Another object is such a system wherein the laser light source is a $CO_2$ laser, a Ruby laser, a long-pulse YAG laser, an Alexandrite laser, an ER:YAG laser, an intense pulsed light laser, a KTP laser, a diode laser, a pulse dye laser or a pulsed Nd:YAG laser. Another object is such a system wherein apparatus is part of a laser scalpel.~~

Please delete the tenth paragraph at page 9, lines 23-24.

Please replace the first full paragraph at page 10, lines 2-3 as follows:

FIG. 9[[C]] B is a photograph of liver cells taken from the biopsy of a dog liver showing full hemangiosarcoma;

Please replace the seventh paragraph beginning at page 10, line 21 continuing onto page 11, line 3 as follows:

The invention is directed to a method and device that does not require the two step process of tissue extraction and analysis before it is determinable whether a tissue mass is malignant. In the method and device of the invention, the spectral data result can be collected and evaluated in real time from a sample *in vivo*. A major advantage of LIBS device and method of the invention is that [[the]] it can be practiced in real-time with either zero or minimal sample preparation.

Please replace the first full paragraph at page 13, lines 3 -11, as follows:

The interaction of high-power laser light with a target sample has been a topic of study in many fields of research and analysis.[[[13,14]]] [6,7] The use of lasers to vaporize, dissociate, excite or ionize species on material surfaces has the potential of becoming a powerful analytical tool. When a high-power laser pulse is focused onto the target of any kind of material (solid, liquid, gas) the irradiation in the focal spot leads to rapid local heating, intense evaporation and degradation of the material. Because a sample of nanograms or micrograms is ablated in a time frame that is roughly in femoseconds to nanoseconds, depending on ~~among other things~~ the laser pulse width, the whole process is considered as non-traumatic.

Please replace the second paragraph at page 13, lines 12-18, as follows:

LIBS is suitable for rapid on-line elemental analysis of different phases of material and has proved its importance in obtaining analytical atomic emission spectra directly from solid, liquid, and gaseous samples. [[[15-18]]][8-11] LIBS has various advantages over conventional laboratory based chemical analysis techniques. It is a sensitive optical technique with high

spatial resolution, in a small focal spot. In the process vaporization and excitation of the sample materials occurs directly in one step.

Please replace the last paragraph beginning at page 13, line 19 continuing onto to page 14, line 7, as follows:

Previous researches have shown significant differences in concentrations of trace elements between normal and cancerous tissue cells. [[[19-20]]]12,13 LIBS, an elemental composition analysis technique, provides useful data to correlate elemental concentration and cancerous tissue cell. Information from the spectra of various cancerous and normal tissues allows the development of this invention for real-time diagnosis of breast cancer. For real-time diagnosis of breast cancer, a micro-size optical fiber probe (probe or micro-probe) using a 500 μm optical fiber. A micro-lens is attached to the tip of the fiber and is used to directly send a pulsed laser beam or spark onto/into a potential breast tumor mass. The light emitted from the tissue mass is carried back to the spectrometer by the same set of optical fibers. The emitted atomic emission from the laser spark is dispersed by the spectrometer and the atomic signature identified. The diagnosis can be achieved in real-time, directly in the patient, optionally using a local anesthetic.

Please replace the last paragraph at page 14, lines 19-24, as follows:

The invention, according to another embodiment, uses an optical fiber bundle for delivering the pulsed laser power to produce a spark as well as for collecting the resulting emission from the spark for quantitative elemental analysis with greater accuracy and a lower detection limit. [[[17]]]10 The optical fiber bundle can, for instance, consist of a central fiber and a ring of surrounding fibers. Other configurations can be determined by those skilled in the art.

Please replace the last paragraph beginning at page 15, line 16 continuing onto page 16, line 3, as follows:

A broad schematic diagram of a micro-probe sensor setup is shown in Figure 1 with a Data Acquisition/Analysis System, an LIBS System, a Probe and Sample. A more detailed schematic diagram of the LIBS optical mechanism is shown in Figure 2 in which a pulsed laser from a [[D]]Nd:YAG Laser system is directed into the optical fiber probe using two mirrors. The harmonic separator mirror reflects the laser beam into the dichroic mirror (DM) which reflects the beam through a lens to the probe cap and onto the specimen. The light emission from the laser-produced plasma on the specimen is collected by a set of lens and passed to the fiber optic bundle which transmits the LIBS signal to the detection system, a spectrograph. A gated intensified charge coupled device is used as the detector with its controller. Computer software can assist the operator to identify and/or quantify the elements present in the sample.

Please replace the second full paragraph at page 16, lines 6-11, as follows:

In Figure 10A, a fiber carrying an intense laser light is directly pointed at the sample tissue cells. Because of the high intensity of the laser beam, the laser induced breakdown takes place and the corresponding LIBS signal is carried back to the spectrometer. This type of arrangement is known for the analysis of solid material submersed in water or other liquid [[$^{14}$]]$^{7}$ but it has not been previously demonstrated with a biological sample.

Please replace the third full paragraph at page 16, lines 12-15, as follows:

Another schematic, as shown in Figure 10B, incorporates a fiber having micro-lens on its tip facing the sample surface. Using this type of arrangement it is [[be]] possible to focus the

laser beam precisely on the surface of the tissue sample. Hence, an increased spatial precision can be achieved.

Please replace the fourth full paragraph at page 16, lines 16-20, as follows:

In a third schematic, as shown in Figure 10C, an optical fiber as in Figure 10A (not shown), or an optical fiber with a micro-lens as in Figure 10B (shown), can be inserted in a needle that is used to guide the fiber to the deep lying tissues in a bulk of human tissue cells. For physicians this schematic is well suited so that an optical fiber can be inserted within the fiber-carrying needle to the suspected cancerous area.

Please replace the first full paragraph at page 17, lines 3-7, as follows:

Preliminary experiments on a canine haemangiosarcoma have been completed. Figures 3A and 3B align the spectra of normal tissue with the spectra of malignant tissue. It is clear that the line intensities of calcium (Figure 3A) and iron (Figure 3B) are lower in the spectrum for neoplastic tissue. Also aluminum (Figure 3A) is present in the normal tissue but not on the neoplastic tissue.[[[15]]][8]

Please replace the last paragraph beginning at page 17, line 20 continuing on to page 18, line 16, as follows:

LIBS spectrum is also used, according to the invention, to identify the source of a sample and for other forensic uses. An LIBS spectrum for hair is shown in Figure 6. The lines for magnesium, calcium, carbon and sodium are very strong, and the lines for sodium and potassium are very weak. An LIBS spectrum for nail is given in Figure 7. The pattern for Figure 6 and Figure 7 are very similar except that the lines for carbon and magnesium are stronger in

comparison to calcium lines in nail than to [[hose]] those for hair. The spectra of Figures 6 & 7 are recorded under similar experimental conditions at a laser energy of 20 mJ, CCD gate delay of 1 μs and gate width of 10 μs. From the spectra of hair and nail one can observe the similarity of their structure.[[[16]]][9] Performing the LIBS methodology with a nail sample is less cumbersome in comparison to hair because with the large flat area of the nail there is no need for special alignment of the laser focal point to the nail surface as needed in case of hair. Also the nail is firmer and more solid in comparison with hair and the LIBS result is more pronounced. For the nail, intensity is approximately three times that in comparison to hair. In LIBS literature this phenomena is described as the matrix effect.[[[6-7]]][3,4] An LIBS spectrum of chicken blood is shown in Figure 8. In a chicken blood sample, the lines for calcium, sodium, lithium, and potassium are strongly apparent. This can be compared with the lower intensity of other compounds along the spectrum as shown in Figure 8B and the profile can be drawn for either or both parts of this whole spectrum.

Please delete the last three paragraphs beginning at page 20, lines 19-24.

Please replace the first through fifth paragraphs at page 21, lines 1-13, as follows:

[[4]]1. Jemal, A., Murray, T., Samuels, A., Ghafoor, A., Ward, E., Thun, M.J. (2003)[[.]], "Cancer statistics, 2003" CA Cancer J. Clin., Vol. 53, 5-26.

[[5]]2. Cancer Facts and Figures 2003: American Cancer Society, www.cancer.org.

[[6]]3. Srinivas, P. R., Srivastava, S., Hanash, S., Wright Jr., G. L., (2001)[[.]], "Proteomics in Early Detection of Cancer", Clin. Chem., 47:10, 1901-1911.

[[7]]4. Ramanujam, N., Chen, J.X., Gossage, K., Kortum, R.R. and Chance, B., (2001)[[.]], "Fast and Noninvasive Fluorescence Imaging of Biological Tissues *in vivo* using a Flying-Spot Scanner", IEEE Trans. on Biomed. Engg., Vol. 48, No. 9, 1034-1041.

[[8]]5. Ntziachristos, V., Brenner C., and Weissleder, R., (2003)[[.]], "Fluorescence imaging with near-infrared light: new technological advances that enable *in vivo* molecular imaging", Eur. Radiol., Vol 13, 195-208.

Please delete the sixth through ninth paragraphs at page 21, lines 14-20.

Please replace the last paragraph at page 21, lines 21-23, as follows:

[[13]]6. Yueh, F.Y., Singh, J.P., and Zhang, H. "Elemental Analysis with Laser Induced Breakdown Spectroscopy", In Encyclopedia of Analytical Chemistry, John Wiley and Sons. Ltd, Chisheter, U.K., 2000.

Please replace the first through the seventh paragraphs at page 22, lines 1-15, as follows:

[[14]]7. Radziemski, L J., and Cremers, D. A. (1989). "Laser Induced Plasma and Applications[[.]]," Marcel Dekker, New York, NY.

[[15]]8. Thiem, T. L., Salter, R. H., Gardner, J. A., Lee, Y. I., and Sneddon, J. (1994)[[.]], Appl. Spectrosc., 48, 58.

[[16]]9. Rusak, D.A., Castle, B.C., Smith, BW., and Winefordner, J.D. (1997)[[.]], Crit. Rev. Anal. Chem., 27, 257.

[[17]]10. Rai, A.K., Yueh, F.Y., and Singh, J.P. (2002)[[.]], "High Temperature Laser-Induced Breakdown Spectroscopy for analysis of molten Alloy constituents" Rev. Sci. Instrum. 73, 3589-3599.

[[18]]11. Samek, O., Beddows, D.C.S., Kaiser, J., Kukhlevsky, S. V., Liska, M., Telle, H.H., and Young, J., (2000)[[.]], Opt. Eng. 38, 2248.

[[19]]12. Kwaitek, W.M., Drewniak, T., Lekka, M., Wajdowicz, A., (1996) Nuclear Instruments and Methods in Physics Research B 109/100 284-288.

[[20]]13. Nidal M. Ershaidat and Sami H. Mahmood, See http://conference.ke.jp/JASS02/26_nidal.pdf.

Please delete the eighth through the tenth paragraphs at page 22, lines 16-24.

## IN THE DRAWINGS

Original FIG 9 includes three black and white photographs (FIGs 9A, 9B and 9C). The change for the replacement removes FIG 9B from the original and FIG 9C from the original is renumbered as FIG 9B.

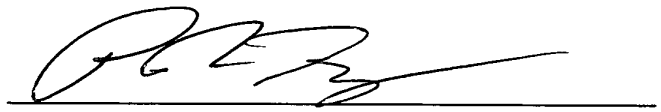
## REMARKS

The specification has been amended to remove select sections not central to the invention or to correct minor editorial matters. The amendment to replace the paragraph at page 3, line 21 to page 4, line 4 merely clarifies what is known in the prior art. The replacement for FIG 9 merely removes FIG 9B and renumbers FIG 9C to become FIG 9B. There are no amendments to the claims. Accordingly, no new matter is introduced by this Preliminary Amendment.

If any issues remain to be addressed in this matter, which might be resolved by discussion, the Examiner is respectfully requested to call Applicants' undersigned counsel at the number indicated below.

Respectfully submitted,

PIPER RUDNICK LLP



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